REMARKS

CLAIM REJECTIONS - 35 U.S.C. §102

Claims 1-3, 9-10 and 16 were rejected under 35 U.S.C. §102 (e) as anticipated by Baugh et al. (U.S. Patent 6,656,919).

The Examiner stated that:

> Claims recite a method to simultaneously or sequentially germinate and kill biological spores via treating said sores with a germinant comprising water, dipicolinic acid and calcium as calcium chloride and a germicidal solution that comprises a peroxygen compound.
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> Baugh et al. teach a method to disinfect or sterilize surfaces or materials contaminated with one or more members selected from bacteria or bacterial spores, wherein *Bacillus cereus* or *Bacillus anthracis* spores are rendered harmless or lifeless or sterilized by subjecting said spores simultaneously to a germinant and a germicidal solution. Alternatively, said spores are first treated with said germinant solution and subsequently with said germicidal solution. This one or two-step process kills said bacterial spores (Column 5, Lines 14-24, 30-35 and 48-58) and sterilizes the surface contaminated with bacterial spores. Said germinant solution comprises one among: adenine, L-alanine, calcium, dipicolinate, glucose and various organic or inorganic anions, and cations in distilled water. Baugh et al. further teach that upon contact with a germinant that does not initially contain dipicolinic acid, with induction of germination, dipicolinic acid is released from the spores into the germinant solution and acts as a germinant for remaining un-germinated spores (Column 7, Lines 30-33). Thus, inherently also Baugh et al's germinant solution comprises dipicolinic acid, calcium as calcium chloride and water concentration in range of 50 to 98 weight percent. Additionally, said germicidal solution comprises art-known bactericidal compound/ compounds or mixtures of such compounds with surfactants and peroxide compounds (e.g., benzoyl and hydrogen peroxides, see Baugh et al., Column 8, Line 26 to Column 12, Line 55). In microbiological art, bacterial spores are recognized as biological spores. Thus, Baugh et al. teach a method to sterilize materials or surfaces contaminated with biological spores comprising same steps and components as are recited in the instantly claimed invention.
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> Therefore, the reference deems to anticipate the cited claims.

Applicants have amended the present application to more fully claim their invention. In light of the instant amendment, Applicants respectfully disagree that Baugh et al. anticipate the present invention.

Applicants' invention is directed to "rapid decontamination" (Specification at page 6, line 13) of a contaminated area (Specification at page 4, line 17) particularly for applications related to the military operations and the like (Specification at page 6, line 19 to page 7, line 15). This rapid decontamination is accomplished using the combination of specific concentrations of dipicolinic acid and calcium ions. In contrast, the method disclosed in Baugh et al. does not address this rapid decontamination (although Baugh et al. states "a process and product for the rapid decontamination of bacterial endospores" see Baugh et al. at col. 7, lns. 5-7), teaching instead germicidal solution that "induces germination in a high percentage of the spores and the germinating spores release dipicolinic acid which act as a additional germinant for any remaining spores" (Baugh et al. at col. 7, lns. 28-33). Additionally in Baugh et al., "[a]ny chemical that induces activation-germination of bacterial endospores can be utilized" (Baugh et al. at col. 8, lns. 14-15), such as "glucose, adenosine, inosine, L-alanine, Calcium dipicolinate, various inorganic cations and anions, and complex bacterial media such as peptone, tryptone, and yeast extract" (Baugh et al. at col. 8, lns. 15-19). As such, Baugh et al. does not teach dipicolinic acid in combination with calcium ions at quantities that provide for rapid decontamination of biological spores, as taught by the present invention. Baugh et al.'s disclosure further teaches away from the present invention by listing the combination of dipicolinic acid and calcium ions as equivalent to other germinants.

Applicants submit, herewith, a Declaration by Inventor Amanda S. Schilling, detailing the

differences between various prospective germinants. Applicants have surprisingly discovered that the use of dipicolinic acid and calcium ions, in the claimed molar amount, is significantly superior for rapid decontamination over other germinants within a decontaminating composition. As detailed in the attached 1.132 Declaration ("Schilling Declaration"), submitted by Inventor Amanda S. Schlling, while conducting research on the instant invention, Inventor Schilling's team focused on the dipicolinic acid/calcium ion germinant because of its superior performance for rapid decontamination. As seen in Table 1 of the Declaration, only combinations of dipicolinic acid and calcium ion provided superior rapid germination and not all concentrations of dipicolonic acid and calcium ions were superior to other prospective germinants, as seen for DPA-Ca (0.6 mM) after 15 minutes having a germination (%) of 67.17. Additionally, the use of other germinants with the dipicolonic acid/calcium ions appeared to be detrimental to the efficient germination resulting from the dipicolonic acid/calcium ions, e.g., 2X LB + Ca-DPA 60 mM having a 98.44% germination compared to DPA-Ca (60 mM) having a 100.00% germination (both at 15 minutes). The data in Table 1 demonstrates that, for rapid decontamination, the application of a given strength of dipicolinic acid and calcium ions is needed, as specified by the present patent application.

CLAIM REJECTIONS - 35 U.S.C. §103

Claims 1-16 were rejected under 35 U.S.C. §103 (a) as obvious over Baugh et al. (U.S. Patent 6,656,919) in view of Paidhungat et al. (Journal of Bacteriology 2000, Volume 182, Pages 2513-2519) and Baker, et al. (U.S. Patent 6,506,803).

The Examiner stated that:

> Claims recite a method to simultaneously or sequentially germinate and kill

biological spores via treating said sores with a germinant comprising dipicolinic acid and calcium and a germicidal solution, wherein the germinant solution comprises 50-90 mM of each one of calcium ions and dipicolinic acid. The compositions administered in said method also comprise a germicidal solution, a surfactant comprising at least one carbon chain of at least ≥ six carbon members, a peroxide compound and an enzyme.

Teachings from Baugh et al. have already been discussed *supra*. Baugh et al., in their method of simultaneously germinating and sterilizing *Bacillus* spores further teach that said germicidal composition comprises non-ionic, anionic and cationic surfactants, wherein said non-inoic surfactants are comprised of compounds having carbon chain in range of 8 to 18 carbon atoms (Column 11, Lines 12-64). Since Baugh et al. teach a method, wherein biological spores are simultaneously germinated and killed (Column 13, Lines 31-44) via mixing together a bacterial spore suspension, a germinant solution and a germicidal solution; intrinsically Baugh et al. teach a method to disinfect or sterilize a surface or material via germination and killing biological spores with a composition comprising water, dipicolinic acid, calcium ions (from the germinant solution), anionic, cationic or nonionic surfactant, wherein the carbon chain length of said surfactant compound ranges between 8-18 and a peroxide (e.g., benzoyl or hydrogen peroxide). Please not that carbon chain length in range of 8-18 encompasses carbon chain length of >6 carbon chain length. Furthermore, Baugh et al. also illustrate a method, wherein the same composition is sprayed on a contaminated surface (i.e., agar surface contaminated with bacterial spores) to decontaminate the sterilize said surface (Column 13, Example 6).

Baugh et al., however, do not teach concentrations of dipicolinic acid and calcium, nor an enzyme in their composition.

Paidhungat et al. teach a method to germinate *Bacillus* spores, wherein *Bacillus* spores are added to a germinant comprising a calcium (i.e., Ca^{2+})-dipicoinic acid (i.e., DPA) concentration in range of <20 mM to 90 MM with highest germination when the concentration of each component, i.e. Ca^{2+} and DPA each in the germinant was equimolar at 60 mM (Page 2517, Column 2, lines 17-29 under Table 4 and Figure 4).

Baker et al. teach a method and a composition to inactivate/decontaminate bacterial cells and spores by exposing them to an oil-in-water emulsion comprising water, a surfactant, oil, an enzyme and a buffer (Abstract, Lines 1-7; Column 5, Lines 12-15; Column 12, Lines 7 -64; Column 18, Lines 18-20; Column 21, Lines 1-32; Column 22, Lines 27-40).

Thus, an artisan of ordinary skill, at the time that said invention was made would be motivated to combine the teachings from each one of the cited references to develop a method to decontaminated or sterilize a material or a surface by either simultaneous or sequential application of a germinant solution and a germicidal solution, because Baugh et al. reference teaches the general principle of germinating and killing biological spores and Baugh et al. further teach either simultaneous or sequential killing of said germinated biological spores, wherein said germinant solution comprises dipicolinic acid and calcium ions and said germicidal solution comprising a peroxide solution and an anionic, cationic or nonionic surfactant with carbon chain length of said surfactant ranges between 8-18; Paidhungat et al. teach that concentration of each of dipicolinic acid and calcium ions in said germinant solution ranges between 20 to 90 mM and the optimal concentration of each of dipicolinic acid and calcium ions in said germinant solution is 60 mM, and Baker et al. teach a method and a composition to inactivate bacterial/fungal spores (i.e., biological spores), wherein said composition comprises water, surfactant and an enzyme. Thus, Paidhungat et al. remedy to deficiency of concentration of each of dipicolinic acid and calcium ions in the teachings from Baugh et al. and Baker et al. remedy the deficiency of an enzyme and a surfactant in the germinant composition from Baugh et al.

It would have been obvious to one or ordinary skill in the art at the time the invetnion was made to modify the method and composition of Baugh et al., according to the teachings from Paidhungat et al. and Baker et al., because Baugh et al. teach the general principle of first germinating the biological spore, wherein biological spores are simultaneously/sequentially germinated and killed. Paidhungat et al. remedy the deficiency of optimal concentration (i.e., 60 mM for each component) of dipicolinic acid and calcium ions in Baugh et al's composition and method, and Baker et al. remedy the deficiency of enzyme and surfactant in the disinfectant composition of Baugh et al.

None of the above discussed prior art references teach the exact same concentration fro water, dipicolinic acid or surfactant on weight basis of the total composition. However, the adjustment of particular conventional working conditions (e.g., the ratios of each one of components in a composition, or their molar concentration etc.) is deemed merely a matter of judicious selection and routine optimization of a result-effective parameter which is well within the purview of the skilled artisan.

From the teachings of the reference cited supra, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima

facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicants respectfully disagree.

Applicants have amended th present application to more fully claim their invention. In light of the instant amendment, Applicants respectfully disagree that the present invention is obvious over Baugh et al. in view of Paidhungat et al. and Baker, et al.

Applicants incorporate, herein, the previous arguments. Additionally, the disclosure of the Paidhungat et al. article focuses on a study to investigate the role of receptor proteins in the spores (*see* Paidhungat et al. at page 2513, column 2, lines 6-16), with the use of dipicolinic acid and calcium ions which have been known to be inherently present in spores populations. As such Paidhunget et al. does not overcome the deficiencies of Baugh et al., as the Paidhungat et al. article does not provide a basis for selection of dipicolinic acid and calcium ions over other types of germinants listed in Baugh et al. In addition to Baugh et al.'s disclosure of "[a]ny chemical that induces activation-germination of bacterial endospores can be utilized" (Baugh et al. at col. 8, lns. 14-15) such as "glucose, adenosine, inosine, L-alanine, Calcium dipicolinate, various inorganic cations and anions, and complex bacterial media such as peptone, tryptone, and yeast extract" (Baugh et al. at col. 8, lns. 15-19), the method taught in Baugh et al. that uses any germinant that "induces germination in a high percentage of the spores and the germinating spores release dipicolinic acid which act as a additional germinant for any remaining spores" (Baugh et al. at col. 7, lns. 28-33) limits the time of germination to at least the germination rate resulting from the wide variety of disclosed germination chemicals of Baugh et al. There is no teaching in Baugh et al. that

selection of specific germinant is desirable, nor is there a teaching in Baugh et al. that the specific concentrations of germinant are desirable. Accordingly, there is no teaching that would motivate one of ordinary skill in the art to vary either the type of germinant or the concentration of the germinant being used.

CLAIM REJECTIONS - 35 U.S.C. §103

Claims 1-16 were rejected under 35 U.S.C. §103 (a) as obvious over Clouston (U.S. Patent 3,617,178) in view of Paidhungat et al. (Journal of Bacteriology 2000, Volume 182, Pages 2513-2519) and Baker, et al. (U.S. Patent 6,506,803).

The Examiner stated that:

> Clouston teaches a method to simultaneously germinate Bacillus/Clostridal spores present in a liquid or a solid material and sterilize said material. Alternatively, said material is disinfected by a method, wherein bacterial spores are first germinated and in a subsequent step germinated spores are killed by heat, chemical or radiation treatment. In said simultaneous/sequential method of germination and sterilization, the spores are germinated via treating the contaminated material with a hydrostatic pressure in range of 100 psi to 20,000 psi accompanied with simultaneous or subsequent heat (up to 80°C) gamma or UV radiation (Column 1, Line 34 to Column 2, Line 19). Said germination is enhanced with addition of an exogenous anion or cation compound (Column 1, Lines 16-19). Thus, intrinsically, Clouston teaches the general principle of first or simultaneous germinating and killing of bacterial spores to sterilize/decontaminate a liquid/solid contaminated with bacterial spores.
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> Clouston, while teaching enhancement of germination in presence of cation solutes, does not teach dipicolinic acid and calcium, nor a surfactant or an enzyme in the germinant composition. Paidhungat et al's method comprising a germinant containing <20 mM to 90 mM calcium ions and dipicolinic acid to germinate Bacilus spores as well as Baker et al's method and composition to germinate and inactivate bacterial cells and spores by exposing them to an oil-in-water emulsion comprising water, a surfactant, oil, and enzyme and a buffer (Abstract, Lines 1-7; Column 5, Lines 12-15; Column 12, Lines 7 -64; Column 18, Lines 18-20; Column 21, Lines 1-32; Column 22, Lines 27-40) has been detailed supra.

Thus, an artisan of ordinary skill, at the time that said invention was made would be motivated to combine the teachings from each one of the cited references to develop a method to decontaminated or sterilize a material or a surface by either simultaneous or sequential application of a germinant solution and a germicidal solution, because Clouston and Baker et al. teach the general principle of germinating and killing biological spores, Clouston further teaches either simultaneous or sequential killing of said germinated biological spores; Paidhungat et al. teach that a germinant solution to germinate Bacillus spores comprises each of each of dipicolinic acid and calcium ions in said germinant solution ranges between 20 to 90 mM and the optimal concentration of each of dipicolinic acid and calcium ions in said germinant solution is 60 mM, and Baker et al. teach that said germinant solution is comprises of water, surfactant and an enzyme. Thus, Paidhungat et al. remedy to deficiency of concentration of each of dipicolinic acid and calcium ions in Cloustons' teachings and Baker et al. remedy the deficiency of an enzyme and a surfactant in the germinant composition in Clouston's teachings.

It would have been obvious to one or ordinary skill in the art at the time the invention was made to modify Clouston's method and composition according to the teachings from Paidhungat et al. and Baker et al., because Clouston teaches the general principle of first germinating the biological spore and subsequently kill the germinated spores through subjecting said germinated spores to heat, chemical or radiation or alternatively, simultaneously subjecting materials contaminated with biological spores to a pH solution, pressure and heat/radiation or chemical. Paidhungat et al. remedy the deficiency of dipicolinic acid and calcium ions in Clouston's teachings, and Baker et al. remedy the deficiency of enzyme and surfactant in Clouston's method.

None of the above discussed prior art references teach the exact same concentration for water, dipicolinic acid or surfactant on weight basis of the total composition. However, the adjustment of particular conventional working conditions (e.g., the ratios of each one of components in a composition, or their molar concentration etc.) is deemed merely a matter of judicious selection and routine optimization of a result-effective parameter which is well within the purview of the skilled artisan.

From the teachings of the reference cited supra, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicants respectfully disagree.

Applicants have amended the present application to more fully claim their invention. In light of the instant amendment, Applicants respectfully disagree that the present invention is obvious over Clouston in view of Paidhungat et al. and Baker, et al.

Applicants' invention is directed to "rapid decontamination" (Specification at page 6, line 13) of a contaminated area (Specification at page 4, line 17) particularly for applications related to the military operations and the like (Specification at page 6, line 19 to page 7, line 15). This rapid decontamination is accomplished using the combination of specific concentrations of dipicolinic acid and calcium ions. In contrast, Clouston does not address this rapid decontamination and teaches "[c]ompounds such as tyrosine, adenosine, glucose, mannose, l-arginine, l-phenylalanine, l-alanine, l-cysteine, inosine and yeast extract" to initiate germination (see Clouston at col. 4, lns. 21-25). As such, Clouston does not teach dipicolinic acid in combination with calcium ions at quantities that provide for rapid decontamination of biological spores, as taught by the present invention. Clouston's disclosure further teaches away from the present invention by failing to identify the combination of dipicolinic acid and calcium ions as germinants.

Applicants submit, herewith, a Declaration by Inventor Amanda S. Schilling, detailing the differences between various prospective germinants. Applicants have surprisingly discovered that the use of dipicolinic acid and calcium ions, in the claimed molar amount, is significantly superior for rapid decontamination over other germinants within a decontaminating composition. As detailed in the attached 1.132 Declaration ("Schilling Declaration"), submitted by Inventor Amanda S. Schlling, while conducting research on the instant invention, Inventor Schilling's team focused on

the dipicolinic acid/calcium ion germinant because of its superior performance for rapid decontamination. As seen in Table 1 of the Declaration, only combinations of dipicolinic acid and calcium ion provided superior rapid germination and not all concentrations of dipicolonic acid and calcium ions were superior to other prospective germinants, as seen for DPA-Ca (0.6 mM) after 15 minutes having a germination (%) of 67.17. Additionally, the use of other germinants with the dipicolonic acid/calcium ions appeared to be detrimental to the efficient germination resulting from the dipicolonic acid/calcium ions, e.g., 2X LB + Ca-DPA 60 mM having a 98.44% germination compared to DPA-Ca (60 mM) having a 100.00% germination (both at 15 minutes). The data in Table 1 demonstrates that, for rapid decontamination, the application of a given strength of dipicolinic acid and calcium ions is needed, as specified by the present patent application.

Additionally, the disclosure of the Paidhungat et al. article focuses on a study to investigate the role of receptor proteins in the spores (*see* Paidhungat et al. at page 2513, column 2, lines 6-16), with the use of dipicolinic acid and calcium ions which have been known to be inherently present in spores populations. As such Paidhunget et al. does not overcome the deficiencies of Clouston, as the Paidhungat et al. article does not provide a basis for selection of dipicolinic acid and calcium ions over the germinants listed in Clouston. There is no teaching in Clouston that selection of specific germinant is desirable, nor is there a teaching in Baugh et al. that the specific concentrations of germinant are desirable. Accordingly, there is no teaching that would motivate one of ordinary skill in the art to vary either the type of germinant or the concentration of the germinant being used.

Examiner's Comments in Paragraph 11 of the Office Action

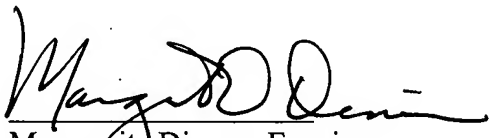
Applicants appreciate the Examiner's comments in paragraph 11 of the Office Action. The

comments discuss matters of law applicable to previous rejections that have not been maintained in the present Office Action. As Applicants believe that the paragraph 11 comments have been forwarded by the Examiner exclusively for clarification to Applicants as to the Examiner's position on certain matters of law regarding the previous rejections, Applicants are not specifically addressing the Examiner's comments, herein.

Applicants respectfully request reconsideration of the instant claims, withdrawal of the rejections cited in the Office Action, and allowance of the instant claims.

The Examiner is invited to contact the attorney of record, listed below, with any questions or other matters to advance the prosecution of the present application.

Respectfully submitted,



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